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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : David J. Pinsky et al.  
Serial No. : 08/721,447  
Filed : September 27, 1996  
For : METHODS FOR TREATING AN ISCHEMIC DISORDER  
AND IMPROVING STROKE OUTCOME

JUL 10 1997

GROUP 1000

1185 Avenue of the Americas  
New York, New York 10036  
June 16, 1997

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. § 1.56, applicants would like to direct the Examiner's attention to the following references which are listed on Form PTO-1449, attached hereto as Exhibit 1. Copies of the references listed below as items 1-19 are attached hereto as Exhibits 2-20, respectively.

1. Connolly et al. (1996) Cerebral protection in homozygous null ICAM-1 mice after middle cerebral artery occlusion, *J. Clin. Invest.* 97, 209-216 (Exhibit 2);
2. Pinsky et al. (1996) Hypoxia-induced exocytosis of endothelial cell Weibel-Palade bodies, a mechanism for rapid neutrophil recruitment after cardiac preservation, *J. Clin. Invest.* 97, 493-500 (Exhibit 3);
3. Connolly et al. (1996) Procedural and strain-related variables significantly affect outcome in a murine model of focal cerebral ischemia, *Neurosurgery* 38, 523-532 (Exhibit 4);

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4. Benedict et al. (1991) Active site-blocked factor IXa prevents intravascular thrombus formation in the coronary vasculature without inhibiting extravascular coagulation in a canine thrombosis model, *J. Clin. Invest.* 88, 1760-1765 (Exhibit 5);
5. Kim et al. (1995) Adhesive glycoproteins CD11a and CD18 are upregulated in the leukocytes from patients with ischemic stroke and transient ischemic attacks, *J. Neurol. Sci.* 128, 45-50 (Exhibit 6);
6. Mayevsky et al. (1995) Multiparametric monitoring of the awake brain exposed to carbon monoxide, *J. Appl. Physiol.* 78, 1188-1196 (Exhibit 7);
7. Bronner et al. (1995) Primary prevention of stroke, *New Eng. J. Med.* 333, 1392-1400 (Exhibit 8);
8. Fassbender et al. (1995) Circulating selectin- and immunoglobulin-type adhesion molecules in acute ischemic stroke, *Stroke* 26, 1361-1364. (Exhibit 9);
9. Seekamp et al. (1994) Role of selectins in local and remote tissue injury following ischemia and reperfusion, *Am. J. Pathol.* 44, 592-598 (Exhibit 10);
10. Jerome et al. (1994) P-selectin and ICAM-1-dependent adherence reactions: role in the genesis of postischemic no-reflow, *Am. J. Physiol.* 266, H1316-H1321 (Exhibit 11);
11. Schroeter et al. (1994) Local immune responses in the rat cerebral cortex after middle cerebral artery occlusion, *J. Neuroimmunol.* 55, 195-203 (Exhibit 12);

12. Okada et al. (1994) P-selectin and intercellular adhesion molecule-1 expression after focal brain ischemia and reperfusion, *Stroke* 25, 202-211 (Exhibit 13);
13. Dawson and Snyder (1994) Gases as biological messengers: nitric oxide and carbon monoxide in the brain, *J. Neurosci.* 14, 5147-5159, (Exhibit 14);
14. Carlos and Harlan (1994) Leukocyte-endothelial adhesion molecules, *Blood* 24, 2068-2101, (Exhibit 15);
15. Verma et al. (1993) Carbon monoxide: a putative neural messenger, *Science* 259, 381-384 (Exhibit 16);
16. Weyrich et al. (1993) In vivo neutralization of P-selectin protects feline heart endothelium in myocardial ischemia and reperfusion injury, *J. Clin. Invest.* 91, 2620-2629 (Exhibit 17);
17. Brown and Piantadosi (1992) Recovery of energy metabolism in rat after carbon monoxide hypoxia, *J. Clin. Invest.* 89, 666-672 (Exhibit 18);
18. Kochaneck and Hallenbeck (1992) Polymorphonuclear leukocytes and monocytes/macrophages in the pathogenesis of cerebral ischemia and stroke, *Stroke* 23, 1367-1379 (Exhibit 19); and
19. Ishimaru et al. (1991) Effects of successive carbon monoxide exposures on delayed neuronal death in mice under the maintenance of normal body temperature, *Biochem. Biophys. Res. Commun.* 179, 836-840 (Exhibit 20).

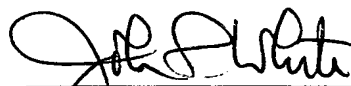
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Applicants maintain that none of the above-listed references citable as a reference against the subject application disclose or suggest the invention now being claimed.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

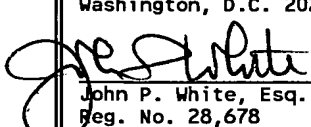
No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:  
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6/16/97  
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